NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of liposuction for chronic lymphoedema

Chronic lymphoedema is the swelling and build-up of body fluid and fat, commonly in the arms and legs, because of problems with the lymphatic system. This procedure uses suction to remove fat tissue and fluid through small cuts in the skin. Afterwards, a compression garment should be worn and only removed for short periods. The aim of the procedure is to reduce the swelling.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in February 2017.

Procedure name

- Liposuction for chronic lymphoedema

Specialist societies

- Royal College of Surgeons of England
- British Association of Plastic, Reconstructive and Aesthetic Surgeons
- The Vascular Society of Great Britain and Ireland
- British Association of Dermatology.

Description

Indications and current treatment

Lymphoedema is the abnormal accumulation of subcutaneous fat and fluid in body tissues that causes swelling. Any part of the body can be affected, but the condition is most common in the arms and legs. Chronic accumulation of lymph leads to hypercellularity, progressive fibrosis and irreversible swelling causing disability, pain and cosmetic issues. Lymphoedema can be complicated by recurrent infection (cellulitis), which further damages the lymphatic vessels and aggravates the condition.

Primary lymphoedema results from a congenital inadequacy and gradual occlusion of lymphatics. Secondary lymphoedema results from damage to the lymphatic system or removal of lymph nodes by surgery, radiation, infection or injury. In the UK, one of the most common types of chronic lymphoedema is secondary lymphoedema of the arm after breast cancer or its treatment. This treatment involves surgery, radiotherapy or both to the lymph glands in the axilla.

Current conservative treatments for lymphoedema include manual lymph drainage (MLD), which stimulates the movement of lymph away from the affected limb, and decongestive lymphatic therapy (DLT). DLT combines MLD massage techniques with compressive bandaging, skin care and decongestive exercises. Once DLT sessions are stopped the patient is fitted with a custom-made compression garment, which is worn every day. These techniques aim to reduce the pain and discomfort associated with lymphoedema.

In very severe cases, surgical treatment can be used to reduce the size of the limb or to restore lymphatic flow. Repeated debulking procedures to excise skin and subcutaneous tissue may be needed. Procedures to restore lymphatic flow from the limb include constructing an alternative lymph drainage pathway via lymphovenous anastomosis.

What the procedure involves

Liposuction for chronic lymphoedema is usually done under general anaesthesia, but regional nerve blockade is also possible. A few small incisions are made in the limb. Cannulas, connected to a vacuum pump, are inserted into the incisions and oedematous adipose tissue is removed by vacuum aspiration. Liposuction is done around and all the way along the limb.

Immediately after liposuction, a compression bandage is applied to the limb to control any bleeding and to prevent postoperative oedema. Antibiotics are typically prescribed after the operation.

The limb is elevated during hospital stay for 3 to 7 days after the procedure. From about 2 weeks after the procedure, a custom-made compression garment is worn. After about 3 months, a new compression garment is custom made. This garment is revised 3 or 4 times during the first year until the oedema volume has been reduced as much as possible and a steady state has been reached.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to liposuction for chronic lymphoedema. The following databases were searched, covering the period from their start to 22 August 2016: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with chronic lymphoedema.
Intervention/test	Liposuction.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 374 patients from 11 case series.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on liposuction for chronic lymphoedema

Study 1 Campisi CC (2016)

Details

Study type	**Case series (retrospective)**
Country	Italy
Recruitment period	Not reported
Study population and number	n=**146**
Age and sex	Age range was: 36 (24.7%) patients had between 20-29 years; 44 (30.1%) 30–39 years; 27 (18.5%) 40–49; 28 (19.2%) 50–59; 11 (7.5%) had more than 60 years. There were 107 (73%) female patients, 58 (35% primary) on the upper limb group and 49 (63% primary) on the lower limb group.
Patient selection criteria	Patients with primary or secondary lymphoedema that had already been treated by lymphatic microsurgery. All patients had residual fibrotic adipose tissue, resistant to conservative treatment. Only patients with unilateral lymphoedema were included as excess volume was compared to the “normal” contralateral limb.
Technique	Fibro-lipo-lymph-aspiration with a lymph vessel sparing procedure. Indocyanine green fluorescent dye and bluer patent violet dye were injected 10 to 15 minutes before the procedure laterally or medially to the main superficial veins at the wrist or ankle on the limb to be treated. This allowed for damage to the lymphatic vessel to be identified in the aspirate. Concomitantly, using a photodynamic camera, the superficial lymphatic network was made visible and sketched onto the skin in indelible ink. After microlymphography, the excess adipose tissue was aspired. Pre- and post-operative excess limb volume was calculated using circumferential measurements and the formula of a frustum. The procedure was done under general anaesthesia when the intervention was done in the upper limb (63 patients). For patients having liposuction on the lower limb either general anaesthesia (55 patients) or selective spinal anaesthesia (28 patients) was used. Tranexamic acid was injected into the treated limb to promote haemostasis. Prophylactic antibiotics were given for 7 days. A compression bandage was used 5 to 7 days post procedure before being replaced with appropriate compression garments. Limb mobilisation was possible 12 hours after surgery.
Follow-up	**1 year**
Conflict of interest/source of funding	None.

Analysis

Follow-up issues: None.
Study design issues:
Study population issues: Forty three patients had upper limb lymphoedema secondary to breast cancer treatments, 20 patients had primary upper limb lymphoedema; 83 patients had lower limb lymphoedema, primary in 49 patients and secondary to cancer surgery in 34.
Other issues: None

Key efficacy and safety findings

<table>
<tr><th>Efficacy</th><th>Safety</th></tr>
<tr><td>n=146
Length of procedure:
• Upper limb – mean 71.5 minutes (45 to 90, SD 13.97)
• Lower limb – mean 105.6 minutes (85 to 120, SD 8.31)

Pre- and post-surgical excess volume
<table><tr><th></th><th>Pre-surgical</th><th>Post-surgical</th><th>p value</th></tr><tr><td>Upper limb</td><td>20%</td><td>3%</td><td><0.001</td></tr><tr><td>Lower limb</td><td>21%</td><td>3%</td><td><0.01</td></tr></table>
All limbs were immediately softer after liposuction and skin changes typical to lymphoedema such as redness, hyperkeratosis and papillomatosis were also normalised.

Sixteen patients (11%) with an almost complete reduction in volume were able to gradually reduce and eliminate the use of compression garments entirely over the 1-year follow-up.</td><td>No patient had evidence of blue dye in the aspirate.
There were no reports of safety events.</td></tr>
<tr><td colspan="2">Abbreviations used: SD, standard deviation</td></tr>
</table>

Study 2 Wojnikow S (2007)

Details

Study type	**Case series (prospective)**
Country	Sweden
Recruitment period	Not reported
Study population and number	n=**80**, 62 with post mastectomy lymphoedema and 18 without lymphoedema (reference group)
Age and sex	Mean 60 years, not stated
Patient selection criteria	Exclusion criteria included a medical or family history of coagulation disorders and of drugs that affected coagulation.
Technique	Patients were divided in 3 groups: - The first (n=19) was operated on without the use of a tourniquet ('dry' technique). - The second group (n=33), liposuction was taken up to the distal edge of the tourniquet, and then the area previously covered by the tourniquet was treated using a 'dry' technique. - The third group (n=10) was treated in the same was as in the second group except that the area covered by the tourniquet was infiltrated with dilute adrenaline before the liposuction was completed (tumescent technique). - Historical reference group (n=18), 9 of whom were treated without dilute adrenaline and 9 treated with it served as controls. Two different wetting solutions were used: - A mixture of 1ml (1mg/ml) adrenaline/1,000ml normal saline (154 mmol/litre, 0.9%) – used in the third group and reference patient group. - A mixture of 2% lignocaine 40 ml, adrenaline 1 ml (1 mg/ml), sodium bicarbonate 25 ml (0.6 mmol/litre, 50 mg/ml), and normal saline 1,000ml – given to the reference group who remained awake and given local anaesthesia The volumes of adrenaline solution injected were equal to or more than the expected volume of aspirate. Forty of the 62 patients with lymphoedema and 4 of the 18 control patients were given general anaesthesia. The remaining patients with lymphoedema were treated with plexus/scalenus blockade and those in the historical group were given local anaesthesia or spinal blockade. In the lymphoedema groups, liposuction was circumferential and done step-by-step from hand to shoulder, with finer cannulas being used for the hands, fingers and the distal part of the forearm. Incisions were left open to drain. Patients with lymphoedema were given cloxacillin or a cephalosporin for 2 weeks following the procedure. In the reference group patients were given only a single dose.
Follow-up	**Perioperative**
Conflict of interest/source of funding	The project was supported by the Tegger Foundation, the Swedish Society of Medicine, the Lundgren Foundation, the Swedish Cancer Society, Stockholm, the Foundation Against Cancer at Malmö University Hospital, the Thureus Foundation at Uppsala University, and Skane County Council's Research and Development Foundation.

Analysis

Follow-up issues: None.

Study design issues: The group not treated with dilute adrenaline overlapped in time with the first group of lymphoedematous patients who were operated on without adrenaline. At that time, we did not use the tumescent technique in our department. The areas treated included the arms, breasts, abdomen, thighs, and hips. All cases were done by the same surgeon.

Study population issues: None.

Other issues: None.

Key efficacy and safety findings

Efficacy

n=**80**, 62 with lymphoedema and 18 without lymphoedema

	Volume of aspirate (ml)	**Mean blood loss, ml (% of total aspirate**
Lymphoedema, no tourniquet, no adrenaline (n=19)	2,471 (1,600 to 3,850)	612 (25%)
Lymphoedema, tourniquet, no adrenaline (n=33)	1,706 (880 to 2,910	225 (13%)
Lymphoedema, tourniquet + adrenaline (n=10)	2,045 (1,340 to 3,370)	100 (5%)
Reference group, with adrenaline (n=9)	2,539 (820 to 4,660)	
Reference group, no adrenaline (n=9)	2,729 (940 to 4,600)	

Safety

Bleeding needing transfusion

	Blood transfusion
Lymphoedema, no tourniquet, no adrenaline (n=19)	37% (7/19)
Lymphoedema, tourniquet, no adrenaline (n=33)	6% (2/33)
Lymphoedema, tourniquet + adrenaline (n=10)	0
Reference group, with adrenaline (n=9)	22% (2/9)
Reference group, no adrenaline (n=9)	7/9

There were no other safety events reported.

Study 3 Brorson H (2006)

Details

Study type	**Case series**
Country	Sweden
Recruitment period	Not stated
Study population and number	n=**49** (35 liposuction and CCT, 14 CCT alone)
Age and sex	Liposuction and CCT – Mean 65 years (SD 12) CCT only – Mean 66 years (SD 13) All females.
Patient selection criteria	Women with arm lymphoedema following breast cancer treatment refractive to manual lymph therapy or pneumatic compression therapy. Lymphoedema was hypertrophic and firm with signs of fibrosis
Technique	CCT sleeve-and-glove garment taken in at each visit using a sewing machine. At the 3, 6 and 12-month visits, a new garment was custom made each time. Patients were also informed of hygiene measures and skin care. Arm volumes were recorded using a water displacement technique. Oedema volume corresponded to the difference between the affected and the 'normal' arm displaced volumes. ROM was measured in degrees with a standard goniometer. • Flexion arm moved in the sagittal plan - (0°= neutral to 180°=normal maximum) • Abduction arm moved away from the side of the body (0°= neutral to 180°= normal maximum) • External rotation (from 0°= neutral to 90°=normal maximum) • Internal rotation (from 0°= neutral to 90°=normal maximum) • Extension arm moved in the sagittal plan (from 0°= neutral to 90°=normal maximum)
Follow-up	**1 year**
Conflict of interest/source of funding	None stated.

Analysis

Follow-up issues: None.

Study design issues: All patients were treated by the same surgeon.

Study population issues: It is uncertain if the population of this paper overlaps with the one from paper 2 as both were produced by the same research group. Treatment was instituted as long as 10 years (mean, range 1 to 43) after mastectomy and radiotherapy.

Other issues: This was 1 of the papers featured in the overview informing the original guidance (IP409).

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>n=49
Oedema volume (ml)
<table><tr><td></td><td></td><td></td><td></td><td colspan="2">Change from baseline</td></tr><tr><td></td><td>Baseline</td><td>6 months</td><td>1 year</td><td>at 6 months</td><td>at 1 year</td></tr><tr><td>LS+CCT</td><td>1,781 (1,528 to 2,080)</td><td>98 (-30 to 230)</td><td>-21(-118 to 113)</td><td>p<0.0001</td><td>0.0001</td></tr><tr><td>CCT</td><td>1,625 (1,350 to 1,968)</td><td>903 (673 to 1,273)</td><td>730 (550 to 1,308)</td><td>p<0.0001</td><td>0.0002</td></tr><tr><td>LS+CCT vs CCT</td><td></td><td></td><td></td><td>p<0.0001</td><td>0.0001*</td></tr></table>Mean volume reduction at 1-year compared with baseline:
• liposuction + CCT = 103%
• CCT alone = 50%
(*Difference between groups at 1-year; p < 0.0001)

Range of motion of shoulder joint
(mean increase in range of motion from baseline to 1 year)
Most measures of range of motion (flexion, extension, abduction, external rotation) increased significantly in both treatment groups (p < 0.05).
Internal rotation increased significantly from baseline in the liposuction + CCT group (p < 0.0001) but not in the CCT alone group.

Subjective outcomes
Symptoms and ADL questionnaire*
Positive differences between baseline and 1-year follow-up for the following subjective quality of life aspects:
<table><tr><td></td><td>Liposuction + CCT</td><td>CCT alone</td></tr><tr><td>Pain</td><td>p<0.0003</td><td>NS</td></tr><tr><td>Swelling of the hand</td><td>p<0.0001</td><td>NS</td></tr><tr><td>ADL difficulties</td><td>p<0.0001</td><td>NS</td></tr><tr><td>Reduced mobility</td><td>p<0.0001</td><td>NS</td></tr><tr><td>Swollen arm</td><td>p<0.0001</td><td>p<0.04</td></tr><tr><td>Heavy arm</td><td>p<0.0001</td><td>NS</td></tr><tr><td>Fatigue/weakness</td><td>p<0.003</td><td>NS</td></tr><tr><td>Numbness</td><td>NS</td><td>NS</td></tr></table>Nottingham Health Profile**
Total score changes:
LS+CCT: 9 (5 to 23) at baseline to 8 (2 to 14) at 1 year , p=0.02
CCT: 14 (8 to 33) at baseline to 15 (6 to 36) at 1 year, not significant.
Significant positive differences between baseline score and 1-year follow-up seen for the following scales of the NHP (p<0.05):
• pain
• physical mobility</td><td>No major surgical complications.</td></tr>
</table>

• housework No significant differences between baseline and 1-year follow-up were seen in the CCT alone group. <u>PGWB</u> (overall) LS+CCT: 107 (100 to 113) at baseline, 109 (100 to 118) at 1 year, p value not significant. CCT only: 101 (89 to 113) at baseline, 106 (90 to 114) at 1 year, p value not significant. There were not statistically significantly differences from baseline to end of follow-up for any of the PGWB dimensions. * VAS (0=no difficulty to 100=extreme difficulty) ** Perceived health problems (0=no problems to 100=all possible problems) *** PGWB – 22 questions rated 1=most negative option to 6=most positive option. Total score maximum 110 points=best achievable well-being.	
Abbreviations used: ADL, activities of daily living; CCT, controlled compression therapy; LS, liposuction; PGWB, psychological general well-being index; VAS, visual analogue scale.	

Study 4 Boyages J (2015)

Details

Study type	**Case series** (prospective)
Country	Australia
Recruitment period	2012 to 2014
Study population and number	n=**21** Patients with primary and secondary lymphoedema attending the advanced lymphoedema assessment clinic at Macquarie University, Australia.
Age and sex	Upper limb group – Mean 57.8 years (12.2) Lower limb group – Mean 50.7 years (16.9) All females.
Patient selection criteria	Eligibility criteria for liposuction included - Unilateral, non-pitting, International Society of Lymphology stage II/III lymphedema - Limb volume difference greater than 25 % - Previously ineffective conservative therapies. Patients were excluded if they had not done maximum DLT (n=3), had active recurrent cancer (n=2), bilateral lymphedema (n=5), frailty (n=3), or were reluctant to wear compression garments continuously (n=5).
Technique	Liposuction was performed under general anaesthesia following limb exsanguination and tourniquet application. Using specialised Helixed Tri Port III cannulas (22 and 30 cm long, 4–5 mm wide) connected to a vacuum pump, subcutaneous tissue was removed through multiple small incisions along the limb. Pre-surgically limb volume determined how much tissue to remove to equalise volume relative to the unaffected limb. Limb volume differences, bioimpedance spectroscopy (L-Dex, assesses extracellular fluid in a unilateral limb using a low-voltage electrical current), symptom and functional measurements using the Patient-Specific Functional Scale were taken before surgery and then at 4 weeks, 3, 6, 9, and 12 months. Compression garments were applied intraoperatively and advised to be worn continuously thereafter.
Follow-up	**1 year**
Conflict of interest/source of funding	None declared. Patients without private health insurance self-funded a 5-day hospital stay, theatre room hire, physiotherapy, and inpatient DLT.

Analysis

Follow-up issues: If progress was good and new garments were not needed, assessment at 3- and/or 9-month was omitted.

Study design issues:

Study population issues: Of 55 eligible patients, 21 had liposuction (15 arm, 6 leg) and had at least 3 months postsurgical follow-up, 18 (85.7%) patients had cancer-related lymphedema.

Other issues: One patient had poor compression garment compliance.

Key efficacy and safety findings

Efficacy

n=**21**, 15 (71%) upper limb, 6 (29%) lower limb

Excess volume and L-Dex value

	Pre-operatively	6 months	1 year	18 months
Overall (n=21)	42.9 (12 to 97)	38.1 (14 to 71), p=0.12	27.1 (13 to 45), p=0.02	–
Upper limb (n)	15	12	7	1
L-Dex[a] (mean, range)	41.2 (18 to 75)	35.3 (14 to 49), p=0.068	25.1 (13 to 45), p=0.018	27
Mean excess value (ml, range)	1,139.5 (645 to 1755)	67.9 (-697 to 422)	18.7 (-244 to 218	-339[b]
Mean excess value (%, range)	44% (27 to 67)	4% (-21 to 21), p<0.001	1% (-5 to 8), p=0.001	-11[b]
Lower limb (n)	6	5	1	0
L-Dex[a] (mean, range)	46.9 (12–97)	49.3 (33–71), p = 0.746	39.0	–
Mean excess value (ml, range)	4058 (2068 to 8294)	400 (-112 to 867)	-103	–
Mean excess value (%, range)	47% (23–83)	4% (-1 to 11), p=0.018	–	–

Functional and emotional impact of lymphoedema

	Pre-operatively	6 months		
	Mean (range)	**Mean (range)**	**n**	**p value**
PSFS functional impairment[1]				
Upper limb	11.1 (4–21)	22.1 (9–30)	7	0.008
Lower limb	7.4 (4–9)	28 (27–29)	5	<0.001
Pain[2]				
Upper limb	3.9 (0–8)	0.8 (0–3)	9	0.007
Lower limb	3.7 (0–8)	0.2 (0–1)	5	0.07
Heaviness[2]				
Upper limb	6.7 (3–10)	0.3 (0–2)	9	<0.001
Lower limb	8.2 (6–10)	0.4 (0–2)	5	0.002
Self-consciousness[2]				
Upper limb	6.9 (2–10)	0.6 (0–3)	9	<0.001
Lower limb	8.2 (4–10)	0 5	24.59	<0.001
Anxious[2]				
Upper limb	5.1 (0–10)	0.2 (0–2)	9	0.11
Lower limb	7.2 (5–10)	0 5	9.36	<0.001
Swollen[2]				
Upper limb	6.9 (2–10)	1.8 (0–4)	9	<0.001
Lower limb	9 (8–10)	1.6 (0–2)	5	<0.001
Impact on emotions[2]				
Upper limb	6 (0–10)	1 (0–4)	9	0.004

Safety

There were no surgical complications.

Lower limb	7.8 (2–10)	0.6 (0–3)	5	<0.001

[a]L-Dex values remained elevated above normal range (0±10) indicating ongoing lymphatic pathology.

[b]Patient gained weight overall but increased in fat volume in the unaffected arm only, the affected arm is now smaller than the unaffected arm.

[1]Scores ranged from '0' (not able to perform three activities at all) to '30' (able to perform three activities perfectly).

[2]Scores ranged from '0' (not at all) to '10' (extremely so)

Abbreviations used: PSFS, patient-specific functional scale.

Study 5 Greene AK (2016)

Details

Study type	**Case series** (retrospective)
Country	USA
Recruitment period	2007 to 2015
Study population and number	n=**15** **Patients with primary and secondary lymphoedema**
Age and sex	Mean 45 years (17-71), 3/15 (20%) males
Patient selection criteria	Patients that had liposuction between 2007 and 2015 that had post-operative follow-up.
Technique	Extremities volumes were calculated using a water displacement and/or circumference measurements based on the formula of a truncated cone. Procedures were performed under general anaesthesia, usually on an outpatient basis. Tumescent solution (1-mg 1:1,000 epinephrine, 50 ml 1% lidocaine in 1 litre of normal saline) was infused into the subcutaneous space, not to exceed 35 mg/kg of lidocaine.
Follow-up	**Mean 3 years**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: None.

Study design issues: None.

Study population issues: Six patients had secondary upper extremity lymphedema after breast cancer treatment, 8 patients had primary lower limb disease, 1 patient had obesity-induced lymphoedema of the leg and 8 patients had a history of repeated cellulitis involving the lymphoedematous extremity.

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **15** <u>Mean lipoaspirate volume</u> Upper limb: 1,612 ml (1,200 to 2,800) Lower limb: 2,902 ml (200-4,800) <u>Mean volume reduction</u> (3-year follow-up) 73% (48 to 94%) All patients reported improved extremity function, reduction in episodes of cellulitis and better quality of life. There was on recurrence at the end of follow-up.	There were 13% (2/15) of patients with severe lower extremity lymphoedema needed a blood transfusion. These patients had a localised skin loss that healed by second intention. One patient had an wound infection needing surgical debridement

Study 6 O'Brien BM (1989)

Details

Study type	**Case series**
Country	Australia
Recruitment period	1986 to 1988
Study population and number	n=**19** patients with primary and secondary lymphoedema (upper limb n=10, lower limb n=9)
Age and sex	Mean 50 years (35–63), 16/19 (84%) females
Patient selection criteria	Patients with primary or secondary chronic lymphoedema.
Technique	Suitable anaesthesia, limb exsanguinated and tourniquet inflated as proximally as possible. Liposuction carried out on half of limb using 6 to 8-mm cannula inserted through 1-cm incisions. Procedure repeated on remaining half of limb. Limb elevated for 2 days postoperatively and custom-made compression garment was worn continuously for the first 6 months, and only by day thereafter.
Follow-up	**10 months** (2 to 15)
Conflict of interest/source of funding	Not stated.

Analysis

Follow-up issues: Of the 19 patients, 2 had their operations close to the publication and follow-up was too short for comment. There were 4 patients from overseers or a geographically distant area and they were lost to follow-up.

Study design issues: Results are not reported separately for patients with primary lymphoedema and those with secondary lymphoedema.

Study population issues: Secondary lymphoedema (n = 14) [breast cancer: 9, melanoma: 3, cervical cancer: 2]; primary lymphoedema (n = 5). The average duration of oedema before liposuction was 11 years (1–23). Seven of the 13 patients who were followed-up were using conservative therapy before liposuction, with elevation and elastic stockings or pumping the limb. Two patients had a second liposuction.

Other issues: This was 1 of the papers featured in the overview informing the original guidance (IP409).

Key efficacy and safety findings

Efficacy	Safety
n=**19** **Oedema volume (n=11)** • Average reduction in limb volume: 23% of excess volume (compared with unaffected limb). • Of 11 patients with unilateral lymphoedema, 10 patients had improved limb volume postoperatively and 1 patient worsened. **Limb size (n=11)** • No reduction in limb size postoperatively: 4 • 1–3 cm reduction in limb size postoperatively: 4 • >3 cm reduction in limb size postoperatively: 3 **Subjective outcomes (n = 13)** • Improved: 11 (patients reported that the limb was lighter and softer). • Stayed the same: 2 patients	No procedural complications reported. Seven patients had cellulitis before procedure. There were 23% (3/13) of patients having cellulitis during follow-up. However, due to short follow-up, it is difficult to assess whether liposuction had an impact on incidence of cellulitis in comparison to preoperative rates.

Study 7 Sando WC (1989)

Details

Study type	**Case series**
Country	US
Recruitment period	Not stated
Study population and number	n=**15** primary and secondary lymphoedema
Age and sex	Age range: 16–70 years , 14 women, 1 man with lymphoedema
Patient selection criteria	Patients with lymphoedema resistant to conservative treatment.
Technique	Water displacement volumetric technique was used in 6 patients. Prophylactic antibiotics were given preoperatively. Suction lipectomy. General anaesthesia. Four to 6 incisions (1 cm) placed along medial or lateral aspects just proximal to knee and ankle or elbow and wrist as appropriate. Five patients treated with additional debulking procedures as part of the same operation. Limb elevated postoperatively, drains removed 5 days postoperatively. Custom-made compression garments worn for at least 3 months postoperatively.
Follow-up	**3 to 30 months**
Conflict of interest/source of funding	Not stated.

Analysis

Follow-up issues:

Study design issues: Results are not reported separately for patients with secondary lymphoedema of the arm and those with primary lymphoedema of the leg.

Study population issues: Five patients had ipsilateral arm swelling after mastectomy for breast cancer, 2 of which also had radiotherapy. Ten patients had lower extremity lymphoedema, of which 6 were idiopathic bilateral, 3 idiopathic unilateral and 1 secondary to groin node dissection for melanoma.

Other issues: Procedure described as ‘suction lipectomy’. This was 1 of the papers featured in the overview informing the original guidance (IP409).

Key efficacy and safety findings

Efficacy	Safety
n=**15** Oedema volume *(measured by water displacement technique)* Average reduction in average limb volume: 1,095 ml (8%) [range: −4,319 ml (decrease) to +1,058 ml (increase)] Limb size Average reduction in average limb circumference: 3 cm (7%) [range: –6.3 cm (reduction) to +0.6 cm (enlargement)] Recurrent lymphoedema - 32% (7/22)[1] at 1-year follow-up. [1]One in the upper limb, 6 in the lower limb.	Three patients had complications: • cellulitis, which resolved with antibiotics • hypaesthesia • marginal wound necrosis (in 1/15 patient having lipectomy combined with debulking)

Study 8 Taylor SM (2011)

Details

Study type	**Case series**
Country	Canada
Recruitment period	Not reported.
Study population and number	n=**10**
Age and sex	Not reported.
Patient selection criteria	Patients with chronic lymphoedema following head and neck cancer surgery.
Technique	All patients had the procedure under local anaesthesia. At the end of the procedure, a compressive facelift dressing is applied and kept for a minimum of 2 days until changed. For a week the tensor bandage is used all the time (with short brakes) but then it can be used only at night for the total of a month. All patients had a week course of antibiotics.
Follow-up	**1 year**
Conflict of interest/source of funding	None.

Analysis

Follow-up issues: None.

Study design issues: None.

Study population issues: All patients had surgery and radiotherapy for head or neck cancer. The cohort had 1 year of cancer free follow-up post liposuction.

Other issues: None.

Key efficacy and safety findings

Efficacy	Safety
n= **10** No patient had recurrence at the end of 1-year follow-up.	There were no adverse events from the procedure.

Efficacy

Oedema volume and limb size

In a case series of 146 patients treated by liposuction for primary or secondary lymphoedema, postoperative limb excess volume was statistically significantly reduced to 3% (from 20% at baseline) in the upper limb group ($p<0.001$) and to 3% (from 21% at baseline) in the lower limb group ($p<0.01$), at 12-month follow-up.[1]

In a case series of 49 patients, 35 patients had liposuction combined with controlled compression therapy (CCT) and 14 had CCT alone. The mean reduction in oedema volume at 12 months compared with baseline was 103% in the combined group and 50% in the CCT alone group (difference between groups $p<0.0001$).[3]

In a case series of 21 patients treated by liposuction, excess volume was statistically significantly reduced in the upper limb group from 1,139 ml (44%) at baseline to 67.9 ml (4%) at 6-month ($p<0.001$) and in the lower limb group from 4058 ml (47%) at baseline to 400 ml (4%) at 6-month follow-up ($p=0.018$).[4]

In a case series of 15 patients treated by liposuction, mean volume reduction of the treated limb was 73% (48 to 94), at the end of the 3-year follow-up.[5]

In a case series of 19 patients (10 with arm lymphoedema and 9 with leg lymphoedema), the average reduction in limb volume after liposuction was 23%. In 1 patient, lymphoedema worsened at the end of the 10-month follow-up. In the same study, 4 patients had no change in circumferential limb size, 4 had a 1–3 cm reduction and 3 had a reduction of more than 3 cm.[6]

In a case series of 15 patients (14 women, 1 man) with chronic lymphoedema treated by liposuction, average reduction in oedema volume was 1,095 ml (−4,319 to 1,058, 8%). In the same case series, average reduction in limb circumference size was 3 cm (−6.3 to 0.6, 7%) at 1-year follow-up.[7]

Recurrent lymphoedema

In the case series of 15 patients (14 women, 1 man) with chronic lymphoedema treated by liposuction, recurrent lymphoedema was reported in 32% (7/22) of patients at 1-year follow-up.[7]

Blood loss

In a case series of 80 patients, mean blood loss as a percentage of the total aspirate was smaller in the group in which a tourniquet and adrenaline were used (100 ml, 5%) than in the group treated with a tourniquet and no adrenaline (225 ml, 13%; no p value reported).[2]

Skin changes

In the case series of 146 patients, limbs were immediately softer after the procedure and redness, hyperkeratosis and papillomatosis were alleviated.[1]

Subjective outcomes

In the case series of 19 patients treated by liposuction, 58% (11/19) of patients reported that the limb was lighter and softer and 11% (2/19) of patients reported no change.[6]

Range of limb movement

In the case series of 49 patients, most measures of range of motion (flexion, extension, abduction, external rotation) increased statistically significantly in both treatment groups ($p<0.05$) when compared with baseline, at 12-month follow-up. In the same study, internal rotation increased statistically significantly from baseline in the liposuction plus CCT group ($p<0.0001$) but not in the CCT alone group.[3]

Lymphoedema associated infection

In the case series of 15 patients treated by liposuction, all patients reported improved extremity function, reduction in episodes of cellulitis and better quality of life.[5]

Use of compression garments

In the case series of 146 patients treated by liposuction, 11% (16/146) of patients were able to completely eliminate the use of compression garment at 1-year follow-up.[1]

Quality of life

In the case series of 49 patients, symptoms and activities of daily living (ADL) were assessed using a visual analogue score (0=no difficulty to 100=extreme difficulty). Pain, swelling of the hand, ADL, mobility, swelling of the arm, heaviness of the arm and fatigue and weakness statistically significantly improved from baseline in the liposuction plus CCT group ($p<0.01$) but not in the CCT alone group (p value non-significant), at 12-month follow-up. In the same study, perceived health problems were assessed using the Nottingham health profile (NHP; 0=no problems to 100=all possible problems). Total score statistically significantly improved in the group treated by liposuction plus CCT, from 9 (range 5 to 23) at baseline to 8 (range 2 to 14) at 12 months ($p=0.02$), but not in the CCT alone group, from 14 (range 8 to 33) at baseline to 15 (range 6 to 36) at 12 months (not significant p value). Other dimensions assessed by the NHP (pain, physical mobility and house work) were statistically significantly

improved from baseline in the patients treated by liposuction plus CCT ($p<0.05$) but not in the group treated by CCT only. In the same study, wellbeing was assessed using the psychological general wellbeing score (total score maximum 110 points=best achievable wellbeing). There were no statistically significantly different differences in the overall well-being score, or individual dimensions between groups, from baseline to 12-month follow-up.[3]

In the case series of 21 patients treated by liposuction, the functional and emotional impact of lymphoedema was assessed using a patient-specific functional scale (overall scores ranged from 0=not able to perform 3 activities at all, 30=able to perform 3 activities perfectly, and individual dimensions scores ranged from 0=not at all, to 10=extremely so). Overall score was statistically significantly improved in the upper limb group from 11.1 (4.0–21.0) at baseline to 22.1 (9.0–30.0) at 6-month follow-up ($p=0.008$), and in the lower limb group from 7.4 (4.0–9.0) at baseline to 28 (27.0–29.0) at 6-month follow-up ($p<0.001$). Individual scores (pain, heaviness, self-consciousness, anxiety, swelling, impact on emotions) were all statistically significantly better at the end of follow-up ($p<0.01$), with exception of anxiety ($p=0.11$) in the upper limb group, and were all statistically significantly improved in the lower limb group ($p<0.01$) at 6-month follow-up.[4]

Safety

Blood transfusion

Blood transfusion was reported in 6% (2/33) of patients in the group treated with a tourniquet, in 37% (7/19) of patients in the group not treated with a tourniquet or adrenaline and in none of the patients in the group treated with a the tourniquet and adrenaline, in a case series of 80 patients treated by liposuction for chronic lymphoedema.[2]

Blood transfusion was reported in 13% (2/15) of patients treated by liposuction in the case series of 15 patients treated by liposuction.[5]

Wound complications

Localised skin loss and healing by second intention was reported in 13% (2/15) of patients in the case series of 15 patients treated by liposuction. Wound infection needing surgical debridement was reported in 1/15 patient in the same case series.[5]

Marginal wound necrosis was reported in 1/15 patient in another case series of 15 patients (14 women, 1 man) with chronic lymphoedema treated by liposuction.[7]

Cellulitis

Cellulitis was reported in 23% (3/13) of patients in the case series of 15 patients treated by liposuction.[6]

Cellulitis was reported in 1/15 patient in the other case series of 15 patients (14 women, 1 man) treated by liposuction.[7]

Other

Hypaesthesia was reported in 1/15 patient in the case series of 15 patients (14 women, 1 man) treated by liposuction.[7]

Validity and generalisability of the studies

- Evidence is made of small non-randomised studies with no long-term follow-up.
- There might be some overlap between papers 2 and 3 in table 2 as both come from the same Swedish center and have close publication date.
- There are technical variations to the procedure that may translate into clinical variability and increase uncertainty.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

NICE guidelines

- Advanced breast cancer: diagnosis and treatment. NICE Clinical Guideline 81 (2009). Last updated July 2014. Available from https://www.nice.org.uk/guidance/cg81
- Early and locally advanced breast cancer: diagnosis and treatment. NICE Clinical Guideline 80 (2009). Available from https://www.nice.org.uk/guidance/cg80

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. XXXX Specialist Advisor Questionnaires for liposuction for chronic lymphoedema were submitted and can be found on the NICE website.

Patient commentators' opinions

Section to be inserted if there is patient commentary

NICE's Public Involvement Programme sent xxx questionnaires to xxx NHS trusts for distribution to patients who had the procedure (or their carers). NICE received xxx completed questionnaires.

Section to be inserted if there is no patient commentary at IPAC 1

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Section to be inserted if there is no patient commentary at IPAC 2

NICE's Public Involvement Programme was unable to gather patient commentary for this procedure.

Section to be inserted if patient commentators raised no new issues

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers.

Section to be inserted if patient commentators raised new issues

The patient commentators raised the following issues about the safety/efficacy of the procedure, which did not feature in the published evidence or the opinions of specialist advisers, and which the committee considered to be particularly relevant:

- [insert additional efficacy and safety issues raised by patient commentators and highlighted by IPAC, add extra rows as necessary].
- [Last item in list].

Company engagement

A structured information request was sent to 4 companies who manufacture a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

- The procedure is followed with non-surgical management, specifically the use of CCT garments. The need for continuing this treatment is not always adequately described, and may be lifelong.

References

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3. Brorson H, Ohlin K, Olsson G et al. (2006) Quality of life following liposuction and conservative treatment of arm lymphedema. Lymphology 39: 8–25.
4. Boyages J, Kastanias K, Koelmeyer LA et al (2015) Liposuction for advanced lymphedema: a multidisciplinary approach for complete reduction of arm and leg swelling. Annals of surgical oncology 22: 1263-1270.
5. Greene AK and Maclellan Reid A (2016) Operative treatment of lymphedema using suction-assisted lipectomy. Annals of Plastic Surgery 77: 337-340.
6. O'Brien BM, Khazanchi RK, Kumar PAV et al. (1989) Liposuction in the treatment of lymphoedema: A preliminary report. *British Journal of Plastic Surgery* 42: 530-533.
7. Sando WC and Nahai F. (1989) Suction lipectomy in the management of limb lymphedema. *Clinics in Plastic Surgery* 16: 369-373.
8. Taylor S and Brake M (2012) Liposuction for the management of submental lymphedema in the head and neck cancer patient. Otolaryngology - Head & Neck Surgery 146: 1028-1030.

Appendix A: Additional papers on liposuction for chronic lymphoedema

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Brake MK, Jain L, Hart RD et al. (2014) Liposuction for submental lymphedema improves appearance and self-perception in the head and neck cancer patient. Otolaryngology - Head and Neck Surgery (United States) 151: 221-225.	Case series n=9 FU= perioperative	Submental liposuction improves the appearance and quality of life for head and neck cancer patients suffering from posttreatment lymphedema by way of improving their self-perception and self-confidence.	Overlaps with paper 11 in table 2, smaller cohort.
Brorson H (2012) Pitting and non-pitting lymphedema: The presence of adipose tissue in lymphedema. European Journal of Lymphology and Related Problems 23: 27-28.	Case series and clinical review 8-year experience	Liposuction can be performed in patients who fail to respond to conservative management or microsurgical reconstruction because the hypertrophy of the subcutaneous adipose tissue cannot be removed or reduced by these techniques. The long-term results of liposuction for chronic large postmastectomy arm lymphedema (17 years) and primary and secondary leg lymphedema (8 years) leading to complete reduction, without recurrence, will be described	Complete overlap with paper 3 table 2. Only outcome reported is limb size reduction.
Brorson H, Ohlin K, Olsson G, et al. (2008) Controlled compression and liposuction treatment for lower extremity lymphedema. Lymphology 41: 52-63.	Case report n=1 FU= not stated	This paper explains our philosophical approach: a pitting lymphedema first should be treated conservatively to remove excess fluid, then liposuction can be performed to remove remaining excess volume bothersome to the patient.	No new safety or efficacy outcomes. Larger sample size papers included in table 2.
Damstra RJ, Voesten HGJM, Brorston H et al. (2009) Circumferential suction-assisted lipectomy for lymphoedema after surgery for breast cancer. BMJ 96: 859-864.	Case series n=35 FU=12 months	Circumferential lipectomy combined with lifelong compression hose is an effective technique in end-stage lymphoedema after treatment for breast cancer.	Overlap with paper 3 table 2. Only outcome reported is limb size reduction.
Doren EL, Smith PD, Sun W al. (2012)	Case series n=6	Six breast cancer survivors had the liposuction procedure from 12/2008-4/2011. Median age was 54 years	No new safety or efficacy outcomes.

Feasibility of liposuction for treatment of arm lymphedema from breast cancer. Cancer Research 72:	FU=15 months (mean)	(range: 43-60) and median volume of fat aspirated was 700mls (range: 350-700). Average volume difference between the affected and unaffected arms at baseline was 522.5 mls (176-867) (geometric) and 589.2mls (280-770) (water displacement). No immediate complications; 1 cellulitis at 4 months post-operative. Average percent volume reductions for 5 of the 6 women at 6 weeks, 6 months and 1 year were 70%, 47%, 71% mls geometrically and 63%, 18%, 54% by water displacement respectively. Quality of life and functionality improved in all patients. Muscle strength remained unchanged. Pain lessened. Average follow-up is 15.49 months (range: 1.8-24.84 months). Conclusion: Liposuction can safely reduce volume of arm lymphedema and improve functionality/quality of life. Larger studies (longer follow-up) are needed to validate the durability of these early results	Larger sample size papers included in table 2.
Eryilmaz T, Kaya B, Ozmen S, and Kandal S (2009) Suction-assisted lipectomy for treatment of lower-extremity lymphedema. Aesthetic Plastic Surgery 33: 671-673.	Case report n=1 FU= not stated	Lymphedema typically occurs on the extremities and affects millions of people throughout the world. Although currently there is no single treatment proven effective for lymphedema in every patient, suction-assisted lipectomy has been shown to be effective in some patients. Suction-assisted lipectomy offers patients with lower-extremity lymphedema a less invasive, less morbid surgical option compared with traditional excisional techniques. In this article we present a case of lymphedema reduction with suction-assisted lipectomy in a patient with bilateral lower-extremity lymphedema.	No new safety or efficacy outcomes. Larger sample size papers included in table 2.
Espinosa-de-Los-Monteros A, Hinojosa CA, Abarca L et al. (2009) Compression therapy and liposuction of lower legs for bilateral hereditary primary lymphedema praecox. Journal of Vascular Surgery 49: 222-224.	Case report n=1 FU= 14 months	No complications were seen and compression therapy was continued. Fourteen month follow-up reveals no increase in leg volume over time, absence of pain, and no further episodes of cellulitis with complete ability to ambulate and return to normal activities. Even when it does not eliminate the underlying cause of primary lymphedema, combined therapy consisting of compression and liposuction is safe and is able to achieve control, at least on a short term, of clinically disabling	No new safety or efficacy outcomes. Larger sample size papers included in table 2.

		conditions associated with advanced stages.	
Kandamany N and Munnoch A (2014) Liposuction for lower limb lipodystrophy in congenital analbuminaemia: A case report. Journal of Plastic, and Reconstructive and Aesthetic Surgery 67: e54-e57.	Case report n=1 FU= 12 months	We have shown that liposuction along with controlled compression therapy is a safe and effective treatment for managing lipodystrophy secondary to congenital analbuminaemia. Although rare, clinicians need to be aware that liposuction is a successful treatment modality, which should be made available to this select group of patients.	No new safety or efficacy outcomes. Larger sample size papers included in table 2.
Leung Nelson, Furniss Dominic, and Giele Henk (2015) Modern surgical management of breast cancer therapy related upper limb and breast lymphoedema. Maturitas 80: 384-390.	Review	Liposuction reduces the volume and symptoms of lymphedema, but needs continual compressive therapy to avoid recurrence. Lymphatic reconstruction or bypass techniques including lymph node transfer (inguinal nodes are transferred to the affected limb), lymphatico-lymphatic bypass (lymphatics bypass the axilla using a lymph vessel graft reconstructing lymphatic flow from arm to neck) and lymphaticovenous anastomoses (lymphatics in the arm are joined to the venous system aiding lymph drainage) show promise in reducing lymphedema significantly. Further research is needed, including into the role of primary lymphaticovenous anastomoses in the prevention of lymphedema at the time of axillary dissection.	Clinical review, reports on papers already included in table 2.
Nicoli F, Constantinides J, Ciudad P et al. (2015) Free lymph node flap transfer and laser-assisted liposuction: a combined technique for the treatment of moderate upper limb lymphedema. Lasers in medical science 30: 1377-1385.			
Qi F, Gu J, Shi Y et al. (2009) Treatment of upper limb lymphedema with combination of liposuction, myocutaneous flap transfer, and lymph-fascia grafting: a	Case series n=15 FU=6 months	A significant decrease of upper limb circumference measurements at all levels was noted postoperatively. Skin tonicity was improved in all patients. Postoperative lymphoscintigraphy revealed reduced lymph stasis. No patient suffered from donor site morbidity. Our results suggest that combining laser liposuction with lymph node flap transfer is a safe and reliable	Larger case series already included, no new safety outcomes.

preliminary study. Microsurgery 29: 29-34.		procedure, achieving a reduction of upper limb volume in treated patients suffering from moderate upper extremity lymphedema	
Schaverien MV, Munro KJ, Baker PA et al. (2012) Liposuction for chronic lymphoedema of the upper limb: 5 years of experience. Journal of Plastic, and Reconstructive & Aesthetic Surgery: JPRAS 65: 935-942.	Case series n=11 FU=26 months	Postoperative measurements in an average of 26 months follow up showed that significant decrease of circumferences of the arms on all levels at surgery side were achieved. The onsets of erysipelas were also reduced. There was no chronic lymphedema found in the donor leg after harvest of the lymph-fascia graft. The results suggest the strategy of liposuction, latissimus myocutaneous flap transfer, and lymph-fascia grafting may provide a useful method for treatment of the chronic upper extremity lymphedema with severe axillary scar contracture.	Larger case series already included, no new safety outcomes.
	Case series n=12 FU=6 months	Our first five years of experience of liposuction combined with application of compression garments has shown significant, reproducible, and stable reduction of upper limb oedema with improvement of overall well-being and reduction in measurable anxiety and depression.	Larger case series already included, no new safety outcomes.

Appendix B: Related NICE guidance for liposuction for chronic lymphoedema

Guidance	Recommendations
NICE guidelines	**Advanced breast cancer: diagnosis and treatment. NICE Clinical Guideline 81 (2009). Last updated July 2014.** 8.1 **Diagnosis and assessment** **Imaging assessment** 8.1.1 Assess the presence and extent of visceral metastases using a combination of plain radiography, ultrasound, computed tomography (CT) scans and magnetic resonance imaging (MRI). **[2009]** 8.1.2 Assess the presence and extent of metastases in the bones of the axial skeleton using bone windows on a CT scan or MRI or bone scintigraphy. **[2009]** 8.1.3 Assess proximal limb bones for the risk of pathological fracture in patients with evidence of bone metastases elsewhere, using bone scintigraphy and/or plain radiography. **[2009]** 8.1.4 Use MRI to assess bony metastases if other imaging is equivocal for metastatic disease or if more information is needed (for example, if there are lytic metastases encroaching on the spinal canal). **[2009]** 8.1.5 Positron emission tomography fused with computed tomography (PET-CT) should only be used to make a new diagnosis of metastases for patients with breast cancer whose imaging is suspicious but not diagnostic of metastatic disease. **[2009]** **Pathological assessment** 8.1.6 Patients with tumours of known oestrogen receptor (ER) status whose disease recurs should not have a further biopsy just to reassess ER status. **[2009]** 8.1.7 Patients with tumours of known human epidermal growth factor receptor 2 (HER2) status whose disease recurs should not have a further biopsy just to reassess HER2 status. **[2009]** 8.1.8 Assess ER and HER2 status at the time of disease recurrence if receptor status was not assessed at the time of initial diagnosis. In the absence of tumour tissue from the primary tumour, and if feasible, obtain a biopsy of a metastasis to assess ER and HER2 status. **[2009]**

Monitoring disease status

8.1.9 Do not use bone scintigraphy to monitor the response of bone metastases to treatment.**[2009]**

8.1.10 Do not use PET-CT to monitor advanced breast cancer. **[2009]**

8.2 **Providing information and support for decision making**

8.2.1 Assess the patient's individual preference for the level and type of information. Reassess this as circumstances change. **[2009]**

8.2.2 On the basis of this assessment, offer patients consistent, relevant information and clear explanations, and provide opportunities for patients to discuss issues and ask questions. **[2009]**

8.2.3 Assess the patient's individual preference for how much they wish to be involved in decision making. Reassess this as circumstances change. **[2009]**

8.2.4 Be aware of the value of decision aids and the range available. Make the most appropriate decision aid available to the patient. **[2009]**

8.3 **Systemic disease-modifying therapy**

8.3.1 Offer endocrine therapy as first-line treatment for the majority of patients with ER-positive advanced breast cancer. **[2009]**

8.3.2 Offer chemotherapy as first-line treatment for patients with ER positive advanced breast cancer whose disease is imminently life-threatening or requires early relief of symptoms because of significant visceral organ involvement, providing they understand and are prepared to accept the toxicity. **[2009]**

8.3.3 For patients with ER-positive advanced breast cancer who have been treated with chemotherapy as their first-line treatment, offer endocrine therapy following the completion of chemotherapy. **[2009]**

Endocrine therapy

8.3.4 Offer an aromatase inhibitor (either non-steroidal or steroidal) to:

- postmenopausal women with ER-positive breast cancer and no prior history of endocrine therapy
- postmenopausal women with ER-positive breast cancer previously treated with tamoxifen. **[2009]**

	8.3.5 Offer tamoxifen and ovarian suppression as first-line treatment to premenopausal and perimenopausal women with ER-positive advanced breast cancer not previously treated with tamoxifen. **[2009]** 8.3.6 Offer ovarian suppression to premenopausal and perimenopausal women who have previously been treated with tamoxifen and then experience disease progression. **[2009]** 8.3.7 Offer tamoxifen as first-line treatment to men with ER-positive advanced breast cancer. **[2009]** **Chemotherapy** 8.3.8 On disease progression, offer systemic sequential therapy to the majority of patients with advanced breast cancer who have decided to be treated with chemotherapy. **[2009]** 8.3.9 Consider using combination chemotherapy to treat patients with advanced breast cancer for whom a greater probability of response is important and who understand and are likely to tolerate the additional toxicity. **[2009]** 8.3.10 For patients with advanced breast cancer who are not suitable for anthracyclines (because they are contraindicated or because of prior anthracycline treatment either in the adjuvant or metastatic setting), systemic chemotherapy should be offered in the following sequence: • first line: single-agent docetaxel • second line: single-agent vinorelbine or capecitabine • third line: single-agent capecitabine or vinorelbine (whichever was not used as second-line treatment). **[2009]** 8.3.11 Gemcitabine in combination with paclitaxel, within its licensed indication, is recommended as an option for the treatment of metastatic breast cancer only when docetaxel monotherapy or docetaxel plus capecitabine are also considered appropriate[4]. **[2009]** **Biological therapy** 8.3.12 For patients who are receiving treatment with trastuzumab[5] for advanced breast cancer, discontinue treatment with trastuzumab at the time of disease progression outside the central nervous system. Do not discontinue trastuzumab if disease progression is within the central nervous system alone. **[2009]** 8.4 **Supportive care**

	8.4.1 Healthcare professionals involved in the care of patients with advanced breast cancer should ensure that the organisation and provision of supportive care services comply with the recommendations made in Improving outcomes in breast cancer: manual update (NICE cancer service guidance [2002]) and Improving supportive and palliative care for adults with cancer (NICE cancer service guidance [2004]), in particular the following two recommendations: • 'Assessment and discussion of patients' needs for physical, psychological, social, spiritual and financial support should be undertaken at key points (such as diagnosis; at commencement, during, and at the end of treatment; at relapse; and when death is approaching).' • 'Mechanisms should be developed to promote continuity of care, which might include the nomination of a person to take on the role of "key worker" for individual patients.' **[2009]** 8.5 **Managing complications** **Lymphoedema** 8.5.1 Discuss with people who have or who are at risk of breast-cancer related lymphoedema that there is no indication that exercise prevents, causes or worsens lymphoedema. **[new 2014]** 8.5.2 Discuss with people who have or who are at risk of breast cancer related lymphoedema that exercise may improve their quality of life. **[new 2014]** 8.5.3 Assess patients with lymphoedema for treatable underlying factors before starting any lymphoedema management programme. **[2009]** 8.5.4 Offer all patients with lymphoedema complex decongestive therapy (CDT) as the first stage of lymphoedema management. **[2009]** 8.5.5 Consider using multilayer lymphoedema bandaging (MLLB) for volume reduction as a first treatment option before compression hosiery. **[2009]** 8.5.6 Provide patients with lymphoedema with at least two suitable compression garments. These should be of the appropriate class and size, and a choice of fabrics and colours should be available. **[2009]** 8.5.7 Provide patients with lymphoedema with clear, written information and the contact details of local and national lymphoedema support groups. **[2009]** **Cancer-related fatigue**

	8.5.8 Offer all patients with advanced breast cancer for whom cancer related fatigue is a significant problem an assessment to identify any treatable causative factors, and offer appropriate management as necessary. **[2009]** 8.5.9 Provide clear, written information about cancer-related fatigue, organisations that offer psychosocial support and patient led groups. **[2009]** 8.5.10 Provide information about and timely access to an exercise programme for all patients with advanced breast cancer experiencing cancer-related fatigue. **[2009]** **Uncontrolled local disease** 8.5.11 A breast cancer multidisciplinary team should assess all patients presenting with uncontrolled local disease and discuss the therapeutic options for controlling the disease and relieving symptoms. **[2009]** 8.5.12 A wound care team should see all patients with fungating tumours to plan a dressing regimen and supervise management with the breast care team. **[2009]** 8.5.13 A palliative care team should assess all patients with uncontrolled local disease in order to plan a symptom management strategy and provide psychological support. **[2009]** **Bone metastases** 8.5.14 Consider offering bisphosphonates to patients newly diagnosed with bone metastases to prevent skeletal-related events and reduce pain. **[2009]** 8.5.15 The choice of bisphosphonate for patients with bone metastases should be a local decision, taking into account patient preference and limited to preparations licensed for this indication. **[2009]** 8.5.16 Use external beam radiotherapy in a single fraction of 8Gy to treat patients with bone metastases and pain. **[2009]** 8.5.17 An orthopaedic surgeon should assess all patients at risk of a long bone fracture, to consider prophylactic surgery. **[2009]** **Brain metastases** 8.5.18 Offer surgery followed by whole brain radiotherapy to patients who have a single or small number of potentially resectable brain metastases, a good

	performance status and who have no or well controlled other metastatic disease. **[2009]** 8.5.19 Offer whole brain radiotherapy to patients for whom surgery is not appropriate, unless they have a very poor prognosis. **[2009]** 8.5.20 Offer active rehabilitation to patients who have surgery and/or whole brain radiotherapy. **[2009]** 8.5.21 Offer referral to specialist palliative care to patients for whom active treatment for brain metastases would be inappropriate. **[2009]** **Early and locally advanced breast cancer: diagnosis and treatment. NICE Clinical Guideline 80 (2009).** **1.1 Referral, diagnosis and preoperative assessment** Patients with symptoms that could be caused by breast cancer are referred by their GP to designated breast clinics in local hospitals (see NICE clinical guideline 27, 'Referral guidelines for suspected cancer'). In addition, women aged between 50 and 70 are invited for screening mammography every 3 years through the NHS Breast Screening Programme (NHSBSP) in England or the Breast Test Wales Screening Programme (BTWSP) in Wales. For most patients, whether they are referred following breast screening or after presentation to a GP, diagnosis in the breast clinic is made by triple assessment (clinical assessment, mammography and/or ultrasound imaging, and core biopsy and/or fine needle aspiration cytology). It is best practice to carry out these assessments at the same visit (see NICE cancer service guidance 'Improving outcomes in breast cancer – Manual update'). **Preoperative assessment of the breast and axilla** 1.1.1 The routine use of magnetic resonance imaging (MRI) of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or ductal carcinoma in situ (DCIS). 1.1.2 Offer MRI of the breast to patients with invasive breast cancer: • if there is discrepancy regarding the extent of disease from clinical examination, mammography and ultrasound assessment for planning treatment • if breast density precludes accurate mammographic assessment • to assess the tumour size if breast conserving surgery is being considered for invasive lobular cancer.

	Preoperative staging of the axilla 1.1.3 Pretreatment ultrasound evaluation of the axilla should be performed for all patients being investigated for early invasive breast cancer and, if morphologically abnormal lymph nodes are identified, ultrasound-guided needle sampling should be offered. **1.2 Providing information and psychological support** 1.2.1 All members of the breast cancer clinical team should have completed an accredited communication skills training programme. 1.2.2 All patients with breast cancer should be assigned to a named breast care nurse specialist who will support them throughout diagnosis, treatment and follow-up. 1.2.3 All patients with breast cancer should be offered prompt access to specialist psychological support, and, where appropriate, psychiatric services. **1.3 Surgery to the breast** **Ductal carcinoma in situ** 1.3.1 For all patients treated with breast conserving surgery for DCIS a minimum of 2 mm radial margin of excision is recommended with pathological examination to NHSBSP reporting standards. Re-excision should be considered if the margin is less than 2 mm, after discussion of the risks and benefits with the patient. 1.3.2 Enter patients with screen-detected DCIS into the Sloane Project (UK DCIS audit)[5]. 1.3.3 All breast units should audit their recurrence rates after treatment for DCIS. **Paget's disease** 1.3.4 Offer breast conserving surgery with removal of the nipple-areolar complex as an alternative to mastectomy for patients with Paget's disease of the nipple that has been assessed as localised. Offer oncoplastic repair techniques to maximise cosmesis. **1.4 Surgery to the axilla** **Invasive breast cancer** 1.4.1 Minimal surgery, rather than lymph node clearance, should be performed to stage the axilla for patients with early invasive breast cancer and no evidence of lymph node involvement on ultrasound or a negative ultrasound-guided needle biopsy. Sentinel lymph node biopsy (SLNB) is the preferred technique. 1.4.2 SLNB should only be performed by a team that is validated in the use of the technique, as identified in the New Start training programme[6].

	1.4.3 Perform SLNB using the dual technique with isotope and blue dye. 1.4.4 Breast units should audit their axillary recurrence rates. **Ductal carcinoma in situ** 1.4.5 Do not perform SLNB routinely in patients with a preoperative diagnosis of DCIS who are having breast conserving surgery, unless they are considered to be at a high risk of invasive disease[7]. 1.4.6 Offer SLNB to all patients who are having a mastectomy for DCIS. **Evaluation and management of a positive sentinel lymph node** 1.4.7 Offer further axillary treatment to patients with early invasive breast cancer who: • have macrometastases or micrometastases shown in a sentinel lymph node • have a preoperative ultrasound-guided needle biopsy with histologically proven metastatic cancer. The preferred technique is axillary lymph node dissection (ALND) because it gives additional staging information. 1.4.8 Do not offer further axillary treatment to patients found to have only isolated tumour cells in their sentinel lymph nodes. These patients should be regarded as lymph node-negative. **1.5 Breast reconstruction** 1.5.1 Discuss immediate breast reconstruction with all patients who are being advised to have a mastectomy, and offer it except where significant comorbidity or (the need for) adjuvant therapy may preclude this option. All appropriate breast reconstruction options should be offered and discussed with patients, irrespective of whether they are all available locally. **1.6 Postoperative assessment and adjuvant therapy planning** **Predictive factors** 1.6.1 Assess oestrogen receptor (ER) status of all invasive breast cancers, using immunohistochemistry with a standardised and qualitatively assured methodology, and report the results quantitatively. 1.6.2 Do not routinely assess progesterone receptor status of tumours in patients with invasive breast cancer.

	1.6.3 Test human epidermal growth receptor 2 (HER2) status of all invasive breast cancers, using a standardised and qualitatively assured methodology 1.6.4 Ensure that the results of ER and HER2 assessments are available and recorded at the multidisciplinary team meeting when guidance about systemic treatment is made. **Adjuvant therapy planning** 1.6.5 Consider adjuvant therapy for all patients with early invasive breast cancer after surgery at the multidisciplinary team meeting and ensure that decisions are recorded. 1.6.6 Decisions about adjuvant therapy should be made based on assessment of the prognostic and predictive factors, the potential benefits and side effects of the treatment. Decisions should be made following discussion of these factors with the patient. 1.6.7 Consider using Adjuvant! Online[8] to support estimations of individual prognosis and the absolute benefit of adjuvant treatment for patients with early invasive breast cancer. 1.6.8 Start adjuvant chemotherapy or radiotherapy as soon as clinically possible within 31 days of completion of surgery[9] in patients with early breast cancer having these treatments. **1.7 Endocrine therapy** **Ovarian suppression/ablation for early invasive breast cancer** 1.7.1 Do not offer adjuvant ovarian ablation/suppression to premenopausal women with ER-positive early invasive breast cancer who are being treated with tamoxifen and, if indicated, chemotherapy. 1.7.2 Offer adjuvant ovarian ablation/suppression in addition to tamoxifen to premenopausal women with ER-positive early invasive breast cancer who have been offered chemotherapy but have chosen not to have it. **Aromatase inhibitors for early invasive breast cancer** 1.7.3 Postmenopausal women with ER-positive early invasive breast cancer who are not considered to be at low risk[10] should be offered an aromatase inhibitor, either anastrozole or letrozole, as their initial adjuvant therapy. Offer tamoxifen if an aromatase inhibitor is not tolerated or contraindicated. 1.7.4 Offer an aromatase inhibitor, either exemestane or anastrozole, instead of tamoxifen to postmenopausal women with ER-positive early invasive breast cancer

	who are not low risk[10] and who have been treated with tamoxifen for 2–3 years. 1.7.5 Offer additional treatment with the aromatase inhibitor letrozole for 2–3 years to postmenopausal women with lymph node-positive ER-positive early invasive breast cancer who have been treated with tamoxifen for 5 years. 1.7.6 The aromatase inhibitors anastrozole, exemestane and letrozole, within their licensed indications, are recommended as options for the adjuvant treatment of early ER-positive invasive breast cancer in postmenopausal women[11]. 1.7.7 The choice of treatment should be made after discussion between the responsible clinician and the woman about the risks and benefits of each option. Factors to consider when making the choice include whether the woman has received tamoxifen before, the licensed indications and side-effect profiles of the individual drugs and, in particular, the assessed risk of recurrence[11]. **Tamoxifen for ductal carcinoma in situ** 1.7.8 Do not offer adjuvant tamoxifen after breast conserving surgery to patients with DCIS. **1.8 Chemotherapy** 1.8.1 Offer docetaxel to patients with lymph node-positive breast cancer as part of an adjuvant chemotherapy regimen. 1.8.2 Do not offer paclitaxel as an adjuvant treatment for lymph node-positive breast cancer. **1.9 Biological therapy** 1.9.1 Offer trastuzumab, given at 3-week intervals for 1 year or until disease recurrence (whichever is the shorter period), as an adjuvant treatment to women with HER2-positive early invasive breast cancer following surgery, chemotherapy, and radiotherapy when applicable. 1.9.2 Assess cardiac function before starting treatment with trastuzumab. Do not offer trastuzumab treatment to women who have any of the following: • a left ventricular ejection fraction (LVEF) of 55% or less • a history of documented congestive heart failure • high-risk uncontrolled arrhythmias • angina pectoris requiring medication • clinically significant valvular disease

- evidence of transmural infarction on electrocardiograph (ECG)
- poorly controlled hypertension.

1.9.3 Repeat cardiac functional assessments every 3 months during trastuzumab treatment. If the LVEF drops by 10 percentage (ejection) points or more from baseline and to below 50% then trastuzumab treatment should be suspended. Restart trastuzumab therapy only after further cardiac assessment and a fully informed discussion of the risks and benefits with the woman.

1.10 Assessment and treatment of bone loss

1.10.1 Patients with early invasive breast cancer should have a baseline dual energy X-ray absorptiometry (DEXA) scan to assess bone mineral density if the:

- are starting adjuvant aromatase inhibitor treatment
- have treatment-induced menopause
- are starting ovarian ablation/suppression therapy.

1.10.2 Do not offer a DEXA scan to patients with early invasive breast cancer who are receiving tamoxifen alone, regardless of pretreatment menopausal status.

1.10.3 Offer bisphosphonates to patients identified by algorithms 1 and 2 in 'Guidance for the management of breast cancer treatment-induced bone loss: a consensus position statement from a UK expert group' (2008)[12] (see appendix 2 of the full guideline).

1.11 Radiotherapy

Radiotherapy after breast conserving surgery

1.11.1 Patients with early invasive breast cancer who have had breast conserving surgery with clear margins should have breast radiotherapy.

1.11.2 Offer adjuvant radiotherapy to patients with DCIS following adequate breast conserving surgery and discuss with them the potential benefits and risks (see recommendation in section 1.3.1)

Radiotherapy after mastectomy

1.11.3 Offer adjuvant chest wall radiotherapy to patients with early invasive breast cancer who have had a mastectomy and are at a high risk of local recurrence. Patients at a high risk of local recurrence include those with four or more positive axillary lymph nodes or involved resection margins.

1.11.4 Consider entering patients who have had a mastectomy for early invasive breast cancer and who are at an intermediate risk of local recurrence into the current UK trial (SUPREMO) assessing the value of

	postoperative radiotherapy. Patients at an intermediate risk of local recurrence include those with one to three lymph nodes involved, lymphovascular invasion, histological grade 3 tumours, ER-negative tumours, and those aged under 40. 1.11.5 Do not offer radiotherapy following mastectomy to patients with early invasive breast cancer who are at low risk of local recurrence (for example, most patients who are lymph node-negative). **Dose fractionation** 1.11.6 Use external beam radiotherapy giving 40 Gy in 15 fractions as standard practice for patients with early invasive breast cancer after breast conserving surgery or mastectomy. **Breast boost** 1.11.7 Offer an external beam boost to the site of local excision to patients with early invasive breast cancer and a high risk of local recurrence, following breast conserving surgery with clear margins and whole breast radiotherapy. 1.11.8 If an external beam boost to the site of local excision following breast conserving surgery is being considered in patients with early invasive breast cancer, inform the patient of the side effects associated with this intervention, including poor cosmesis, particularly in women with larger breasts. **Radiotherapy to nodal areas** 1.11.9 Do not offer adjuvant radiotherapy to the axilla or supraclavicular fossa to patients with early breast cancer who have been shown to be histologically lymph node-negative. 1.11.10 Do not offer adjuvant radiotherapy to the axilla after ALND for early breast cancer. 1.11.11 If ALND is not possible following a positive axillary SLNB or four-node sample, offer adjuvant radiotherapy to the axilla to patients with early breast cancer (see recommendations in sections 1.4.1 and 1.4.7). 1.11.12 Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and four or more involved axillary lymph nodes. 1.11.13 Offer adjuvant radiotherapy to the supraclavicular fossa to patients with early breast cancer and one to three positive lymph nodes if they have other poor prognostic factors (for example, T3

	and/or histological grade 3 tumours) and good performance status. 1.11.14 Do not offer adjuvant radiotherapy to the internal mammary chain to patients with early breast cancer who have had breast surgery. **1.12 Primary systemic therapy** **Early breast cancer** 1.12.1 Treat patients with early invasive breast cancer, irrespective of age, with surgery and appropriate systemic therapy, rather than endocrine therapy alone, unless significant comorbidity precludes surgery. 1.12.2 Preoperative systemic therapy can be offered to patients with early invasive breast cancer who are considering breast conserving surgery that is not advisable at presentation. However, the increased risk of local recurrence with breast conserving surgery and radiotherapy rather than mastectomy after systemic therapy should be discussed with the patient. **Locally advanced or inflammatory breast cancer** 1.12.3 Offer local treatment by mastectomy (or, in exceptional cases, breast conserving surgery) followed by radiotherapy to patients with locally advanced or inflammatory breast cancer who have been treated with chemotherapy. **1.13 Complications of local treatment and menopausal symptoms** **Lymphoedema** 1.13.1 Inform all patients with early breast cancer about the risk of developing lymphoedema and give them relevant written information before treatment with surgery and radiotherapy. 1.13.2 Give advice on how to prevent infection or trauma that may cause or exacerbate lymphoedema to patients treated for early breast cancer. 1.13.3 Ensure that all patients with early breast cancer who develop lymphoedema have rapid access to a specialist lymphoedema service. **Arm mobility** 1.13.4 All breast units should have written local guidelines agreed with the physiotherapy department for postoperative physiotherapy regimens. 1.13.5 Identify breast cancer patients with pre-existing shoulder conditions preoperatively as this may inform further decisions on treatment.

	1.13.6 Give instructions on functional exercises, which should start the day after surgery, to all breast cancer patients undergoing axillary surgery. This should include relevant written information from a member of the breast or physiotherapy team. 1.13.7 Refer patients to the physiotherapy department if they report a persistent reduction in arm and shoulder mobility after breast cancer treatment. **Menopausal symptoms** 1.13.8 Discontinue hormone replacement therapy (HRT) in women who are diagnosed with breast cancer. 1.13.9 Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. HRT[13] may, in exceptional cases, be offered to women with severe menopausal symptoms and with whom the associated risks have been discussed. 1.13.10 Offer information and counselling for all women about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment. 1.13.11 Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer. 1.13.12 The selective serotonin re-uptake inhibitor antidepressants paroxetine[14] and fluoxetine[14] may be offered to women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not to those taking tamoxifen. 1.13.13 Clonidine, venlafaxine[14] and gabapentin[14] should only be offered to treat hot flushes in women with breast cancer after they have been fully informed of the significant side effects. 1.13.14 Soy (isoflavone), red clover, black cohosh, vitamin E and magnetic devices are not recommended for the treatment of menopausal symptoms in women with breast cancer. **1.14 Follow-up** **Follow-up imaging** 1.14.1 Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years. 1.14.2 On reaching the NHSBSP/BTWSP screening age or after 5 years of annual mammography follow-up we

	recommend the NHSBSP/BTWSP stratify screening frequency in line with patient risk category. 1.14.3 Do not offer mammography of the ipsilateral soft tissues after mastectomy. 1.14.4 Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have been treated for early invasive breast cancer or DCIS. **Clinical follow-up** 1.14.5 After completion of adjuvant treatment (including chemotherapy, and/or radiotherapy where indicated) for early breast cancer, discuss with patients where they would like follow-up to be undertaken. They may choose to receive follow-up care in primary, secondary, or shared care. 1.14.6 Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include: • designated named healthcare professionals • dates for review of any adjuvant therapy • details of surveillance mammography • signs and symptoms to look for and seek advice on • contact details for immediate referral to specialist care, and • contact details for support services, for example support for patients with lymphoedema.

Appendix C: Literature search for liposuction for chronic lymphoedema

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	22/08/2016	Issue 8 of 12, August 2016
HTA database (Cochrane)	22/08/2016	Issue 3 of 4, July 2016
Cochrane Central Register of Controlled Trials (Cochrane)	22/08/2016	Issue 7 of 12, July 2016
MEDLINE (Ovid)	22/08/2016	1946 to August Week 2 2016
MEDLINE In-Process (Ovid)	22/08/2016	August 19, 2016
EMBASE (Ovid)	22/08/2016	1974 to 2016 Week 34
PubMed	22/08/2016	n/a
CINAHL (NLH Search 2.0 or EBSCOhost) (delete if not requested)	22/08/2016	EBSCO
BLIC (British Library)	22/08/2016	n/a

Trial sources searched on 16/08/2016

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 16/08/2016

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

The MEDLINE search strategy was adapted for use in the other sources.

Database: Ovid MEDLINE(R) <1946 to August Week 2 2016>

1 Lymphedema/ (7769)
2 lymphoed*.tw. (1721)
3 lymphed*.tw. (5195)
4 Lymphocele/ (856)
5 lymphocel*.tw. (1169)
6 (lymph* adj4 edema*).tw. (997)
7 (fluid adj4 (drain* or block* or retent*)).tw. (7046)
8 (tissue* adj4 (swell* or swollen)).tw. (2230)
9 ((milroy* or meige*) adj4 diseas*).tw. (158)
10 or/1-9 (20889)
11 Lipectomy/ (3054)
12 lipectom*.tw. (636)
13 lipoplast*.tw. (241)
14 lipolysis.tw. (10121)
15 adipectom*.tw. (7)
16 dermolipectom*.tw. (146)
17 (fat* adj4 excision*).tw. (214)
18 Adipose Tissue/su [Surgery] (1493)
19 (adipose tissue adj4 surg*).tw. (222)
20 Surgery, Plastic/ (24972)
21 (plastic adj4 surger*).tw. (12418)
22 liposuct*.tw. (2256)
23 (fat adj4 suction).tw. (62)
24 or/11-23 (46084)
25 10 and 24 (198)
26 Animals/ not Humans/ (4266645)
27 25 not 26 (197)
28 limit 27 to ed=20120911-20160831 (36)